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C.P.F.

To: Dr. G. E. Inskeep Date: July 20, 1977  
From: H. J. Grubbs, T. V. Van Auken and W. R. Johnson  
(Written by: T. V. Van Auken)  
Subject: Rebuttal to Examiner's Comments in U.S. Patent Office Action  
on P.M. 687 C.I.P. (D&O 75-31/III)

The examiner, in this office action, has raised objections to our application in four broad areas: 1) safety and health, 2) vinyl *versus* allyl carbonates, 3) the Lee patent (U.S. 3,306,880), and 4) unsupported claims. All of these objections are rebuttable.

Safety and Health -

In her eagerness to declare that our compounds are unhealthy and unsafe in their intended use, the examiner has exceeded the bound of reason. The compounds which we claim are all substituted vinyl menthyl carbonates. Those will be polymerized and the polymers added to cigarette filler. On pyrolysis menthol is released to smoke. The examiner has claimed that these compounds will release phosgene (dichloro-carbonyl) into smoke. This is chemically impossible. There is no chlorine in any of the monomers (substituted vinyl menthyl carbonates) we claim, nor is there any in the polymers to which the monomers are converted.

The examiner is on equally weak ground in assuming that these materials will release hydrogen cyanide into smoke. The monomers we claim do not contain nitrogen, nor do the polymers to which they are converted. In the Description of the Invention it is mentioned that R, the substituent on the vinyl double bond, may be various nitrogen-containing heterocycles. The chemically most probable pyrolytic fate of these substituent groups would be release of the parent heterocycles. This is a desirable effect since many of these heterocycles are important flavorants. The flat statement by the examiner, unsupported by any chemical evidence, that the nitrogen in these heterocycles will be converted to harmful amounts of hydrogen cyanide will not stand under scientific scrutiny.

Finally, we should point out that the basic purpose of using these materials is to reduce hydrogen cyanide and other gases in cigarette smoke. Activated carbon filters, which are effective in removing hydrogen cyanide from cigarette smoke, cannot be used with menthol cigarettes because on storage the menthol migrates to and is trapped by the active carbon in the filter. By the use of our invention, the menthol is not free

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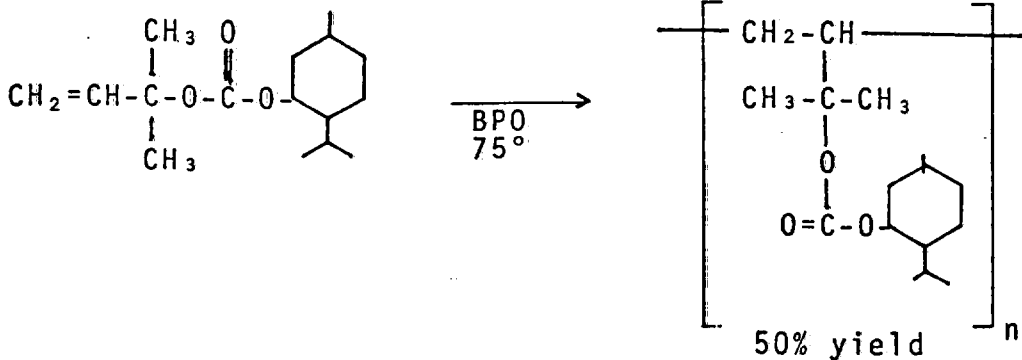
to migrate, and an active carbon filter can be used. In the case at hand, the examiner's objections frustrate her own goals!

The examiner states that we have not provided any enabling support for sulfur-containing heterocycles. This is reasonable since we have not claimed R as a sulfur-containing heterocycle, nor have we mentioned this in the description of the invention.

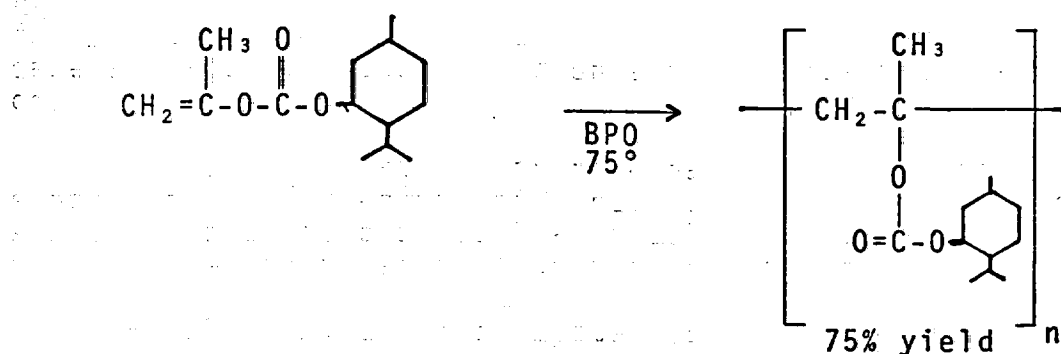
Finally the examiner states (Box 4, lines 8-11), "For example, no enabling support is seen for...substituents which would form poisonous products upon smoking." Obviously, this is correct since we do not claim any substituents which are known to form poisonous products upon smoking.

#### Allyl versus Vinyl Carbonates -

The examiner writes of " $\alpha$ -substituted" and " $\beta$ -substituted" vinyl carbonates and implies that these are clearly related. Actually the correct chemical terms are vinyl carbonates and allylic carbonates, and they are significantly different in their modes of preparation and chemical properties. Tables 1 and 2 show a number of common vinyl compounds and contrast their chemical properties with those of the corresponding allyl compounds. Vinyl compounds are a unique class of compounds, having the hetero atom of the substituent directly attached to a carbon atom which is part of a double bond. Vinyl compounds cannot readily undergo direct substitution reactions (*i.e.*,  $S_N1$  and  $S_N2$ ). They must be made by indirect methods and they polymerize readily. In contrast, allyl compounds readily undergo direct substitution reactions ( $S_N1$ ,  $S_N1'$ ,  $S_N2$ , and  $S_N2'$ ), and in fact they are often prepared by such reactions. Allyl compounds uniformly require more forcing conditions for polymerization and give lower yields than do vinyl compounds. Contrast the polymerization yields of dimethylallyl menthyl carbonate in Rundberg, *et al.*, U.S. 3,887,603, with the polymerization yield of 1-methylvinyl menthyl carbonate in the present application.



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Finally, it should be noted that vinyl carbonates contain a higher weight-percentage of flavorant than do corresponding allylic carbonates, thus requiring less extraneous material.

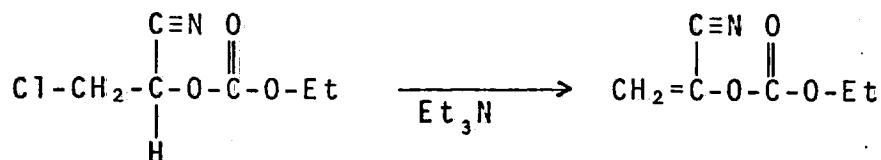


65.0 Weight-Percent Menthol    58.2 Weight-Percent Menthol

The compound claimed and described in the present application are all vinyl compounds. The compounds described in Rundberg, *et al.*, Bayley, *et al.*, (patent examiner's references A and B) are allylic rather than vinyl. Because of their very different chemical properties (esp. preparation and polymerization), they do not make the compounds in the present case obvious at all.

#### The Lee Reference -

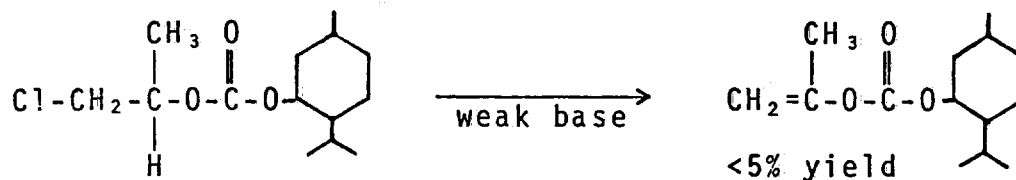
L. H. Lee [U.S. 3,306,880 (Feb. 28, 1967)] prepared 1-cyanovinyl ethyl carbonate by the following reaction:



This reaction is successful in this case because the nitrile group makes the  $\alpha$ -proton more acidic, and thus susceptible to removal by a weak base. When we tried to prepare our carbonates *via* a similar reaction (where R is alkyl and the  $\alpha$ -proton is not acidic), the yield was so low (<5%) as to be totally impractical. Even with a very strong base (potassium *t*-butoxide, sodium methoxide) the yield reached only 20% in one

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case. In the other case, the yield was 0% and starting material completely converted to free menthol. When the exact reagents and conditions described by Lee were used in an attempt to prepare  $\alpha$ -methylvinyl menthyl carbonate, no product at all was obtained. Thus, the method described by Lee is totally inapplicable to the compounds which we claim.



#### Unsupported Claims -

Claims 11 and 12 cover compounds for which there are no working examples in the application. This must represent some kind of oversight since these examples were executed on February 5, 1976 (H. J. Grubbs, Notebook No. 6821, pp. 28-30, 32, 33). These examples are attached. All other compounds appearing in the claims are clearly illustrated by working examples in the application.

#### EXAMPLE NO. XIV:

##### Menthyl $\alpha$ -(4'-Methoxyphenyl)vinyl Carbonate -

Potassium hydride (16.2 g of 24.76 wt-% suspension in mineral oil) was washed with three 250-ml portions of ether, and then suspended in 100 ml of THF which had been distilled from lithium aluminum hydride. This suspension was cooled to 5° and stirred while 15.0 g (0.10 mole) of 4'-methoxyacetophenone in 100 ml of similarly dried THF was added slowly. After gas evolution had ceased, the entire mixture was added rapidly to 20.8 g (0.095 mole) of menthyl chloroformate in 400 ml of THF at 5° with stirring. Cooling was removed, and stirring continued for 1 1/2 hrs. Then 500 ml of ether was added and the mixture was washed with four 500-ml portions of water. The ether solution was then dried over magnesium sulfate. Solvent removal under reduced pressure, gave 31.4 g of crude menthyl  $\alpha$ -(4'-methoxyphenyl)vinyl carbonate as a red oil. This oil was distilled through the molecular still at 75° skin temperature and 0.05 mm pressure to give 27.6 g of colorless liquid. The infrared spectrum indicated a small amount of menthyl chloroformate. A 10 g portion of the material was then distilled through a short adiabatic column equipped with a total reflux head.

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Table I. Preparation and Polymerization of Vinyl Compounds

Compound	Structure	Preparation	Polymerization
Vinyl Chloride	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{Cl} \end{matrix}$	$\text{Cl}-\text{CH}_2\text{CH}_2\text{Cl} \xrightarrow[\text{EtOH}]{\text{K}}$	Suspension Almost 100% yield
Vinyl Methyl Ether	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{O}-\text{CH}_3 \end{matrix}$	$\text{HC}\equiv\text{C}-\text{H} \xrightarrow[2) \text{H}^+]{1) \text{NaOCH}_3}$	High yield Used commercially
Vinyl Acetate	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{O}-\text{C}(=\text{O})\text{CH}_3 \end{matrix}$	$\text{CH}_2=\text{CH}_2 + \text{HOAc} \xrightarrow[\text{CuOAc}]{(\phi_3\text{P})_4\text{Pd}, \text{O}_2}$	Suspension 100%
Vinyl Methyl Carbonate	$\text{CH}_2=\text{CH}\begin{matrix} \text{H} \\ \text{O}-\text{C}(=\text{O})-\text{O}-\text{CH}_3 \end{matrix}$	$\text{Cl}-\text{C}(=\text{O})-\text{O}-\text{CH}_2\text{CH}_2-\text{O}-\text{C}(=\text{O})\text{Cl} \xrightarrow{\Delta} \text{CH}_2=\text{CH}-\text{O}-\text{C}(=\text{O})\text{Cl}$ $\text{CH}_2=\text{CH}-\text{O}-\text{C}(=\text{O})\text{Cl} + \text{NaOMe} \longrightarrow \text{CH}_2=\text{CH}-\text{O}-\text{C}(=\text{O})\text{CH}_3$	Not available
Vinyl Menthyl Carbonate	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{O}-\text{C}(=\text{O})-\text{O}-\text{C}_6\text{H}_{11} \end{matrix}$	$\text{CH}_2=\text{CH}-\text{O}-\text{C}(=\text{O})\text{Cl} + \text{NaO}-\text{C}_6\text{H}_{11} \longrightarrow$	Bulk ~50% (Laboratory only)

Table II. Preparation and Polymerization of Allyl Compounds

Compound	Structure	Preparation	Polymerization
Allyl Chloride	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{CH}_2-\text{Cl} \end{matrix}$	$\text{CH}_2=\text{CH}-\text{CH}_3 \xrightarrow{\text{Cl}_2}$	Low DP (bulk)
Allyl Methyl Ether	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{CH}_2-\text{O}-\text{CH}_3 \end{matrix}$	$\text{CH}_2=\text{CHCH}_2\text{Cl} \xrightarrow{\text{NaOCH}_3}$	Poor by all methods
Allyl Acetate	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{CH}_2-\text{O}-\text{C}(=\text{O})\text{CH}_3 \end{matrix}$	$\text{CH}_2=\text{CHCH}_2\text{OH} + \text{HOAc} \longrightarrow$	50% conversion, slow rates
Allyl Methyl Carbonate	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{CH}_2\text{O}-\text{C}(=\text{O})-\text{O}-\text{CH}_3 \end{matrix}$	$\text{CH}_2=\text{CH}-\text{CH}_2\text{O}-\text{C}(=\text{O})\text{Cl} + \text{CH}_3\text{O}^\ominus\text{Na}^\oplus \longrightarrow$	Low yield, no commercial utility
Allyl Menthyl Carbonate	$\text{CH}_2=\text{C}\begin{matrix} \text{H} \\ \text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{O}-\text{C}_{10}\text{H}_{17} \end{matrix}$	$\text{CH}_2=\text{CHCH}_2\text{O}-\text{C}(=\text{O})\text{Cl} + \text{C}_{10}\text{H}_{17}\text{O}^\ominus\text{K}^\oplus \longrightarrow$	50% yield (bulk) Low DP

DP = Degree of polymerization

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